### SEQUENCE LISTING

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<120> Method for detecting LDI

<120> Method for detecting LDL receptor gene mutations associated with

<130> U 015859-4 <140> 10/542,937 <141> 2006-09-08 <160> 259 <150> ES200300206 <151> 28.01.03 <150> ES200302671 <151> 17.11.03 <210> 1 <211> 60.000 <212> polynucleotide <213> human <220> <221> gene

<223> rLDL <400>

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26110 gtc tgc gat ggc agc gct gag tgc cag gat ggc tct gat gag tcc cag Val Cys Asp Gly Ser Ala Glu Cys Gln Asp Gly Ser Asp Glu Ser Gln 30

gag acg tgc t gtgagtcccc tttgggcatg atatgcattt atttttgtaa 26160

### Glu Thr Cys

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ceg cag ege tgt agg ggt ett tac gtg tte caa ggg gae agt age eec

150

145

Trp Ala Cys Asp Asn Asp Pro Asp Cys Glu Asp Gly Ser Asp Glu Trp

155

31221

31269

015859-4.ST25.2008-12-10.SEQ LISTING Pro Gln Arg Cys Arg Gly Leu Tyr Val Phe Gln Gly Asp Ser Ser Pro 170 31317 tgc tcg gcc ttc gag ttc cac tgc cta agt ggc gag tgc atc cac tcc Cys Ser Ala Phe Glu Phe His Cys Leu Ser Gly Glu Cys Ile His Ser 185 190 180 31365 age tgg ege tgt gat ggt gge eee gae tge aag gae aaa tet gae gag Ser Trp Arg Cys Asp Gly Gly Pro Asp Cys Lys Asp Lys Ser Asp Glu 200 205 31415 Glu Asn Cys 210 ctgtccctgg gctccccag gtgtgggaca tgcagtgatt taggtgccga agtggatttc 31475 caacaacatg ccaagaaagt attcccattt catgtttgtt tetttttttt ettttettte 31535 tttattttgt ttttgagatg gagteteaet etgtgatttt ttteatetet aaattteeta 31595 catccatatg gccaccatga ggccccaggc tggccgatgg ttgctgttag cttattggga 31655 aatcactgtt tggaaggtgc tggttgtttt ttgttgtttg ttgtttttgt ttttgttttt 31715 gttttgagac ggagtetege tetgtegeca gggtggagtg eagtggegeg ateageteae 31775 tgcaacetee getteetggg ttcaageeat teteetgeet eageeteeca agtagegegg 31835 attacaggca tgtgccacca cctccggcta tttttttttc tatttagtag agatggggtt 31895 teaceatgtt agteaggetg gteatgaact ettgacetea ggtgateeae eegeetegge 31955 ctcccaaagt gctgggatta caggcgtgca ctgctgcacc cagccttttt ttgttttttt 32015 gagacagggt cttgctgtca cccaggttga agtaaggtgg cacgattatg gctcactgcg 32075 gcettgatet cettggetea agegateete teaetteage eteteaagea gttggaacea 32135 caggetgtac caccaageet ggccaatttt tttgtacaga cacaggetgg tettgaacte 32195 ctgggctcaa gcaatcctcc tgccttggcc tcccaaagtg ctgggattcc aggcatgagc 32255 egetgeacce ggeaaaagge eetgettett tttetetggt tgtetettet tgagaaaate 32315 32365 aacacactet gteetgtttt eea get gtg gee aec tgt ege eet gae gaa Ala Val Ala Thr Cys Arg Pro Asp Glu 215 32413 ttc cag tgc tct gat gga aac tgc atc cat ggc agc cgg cag tgt gac Phe Gln Cys Ser Asp Gly Asn Cys Ile His Gly Ser Arg Gln Cys Asp 235 230 225 220 32461 cgg gaa tat gac tgc aag gac atg agc gat gaa gtt ggc tgc gtt aat Arg Glu Tyr Asp Cys Lys Asp Met Ser Asp Glu Val Gly Cys Val Asn 250 245 g gtgagegetg gecatetggt ttteeateee eeattetetg tgeettgetg 32512 cttgcaaatg atttgtgaag ccagagggeg etteeetggt eagetetgea ecagetgtge 32572

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ctc tgc gag gga ccc aac aag ttc aag tgt cac agc ggc gaa tgc atc 33219 Leu Cys Glu Gly Pro Asn Lys Phe Lys Cys His Ser Gly Glu Cys Ile 255 260 265

255 260 265
acc ctg gac aaa gtc tgc aac atg gct aga gac tgc cgg gac tgg tca 33267
Thr Leu Asp Lys Val Cys Asn Met Ala Arg Asp Cys Arg Asp Trp Ser
270 275 280 285

gat gaa ccc atc aaa gag tgc g gtgagtctcg gtgcaggcgg cttgcagagt 33319 Asp Glu Pro Ile Lys Glu Cys

290

ttgtggggag ccaggaaagg gactgagaca tgagtgctgt agggttttgg gaactccact 33379 ctgcccaccc tgtgcaaagg gctccttttt tcattttgag acagtctcgc acggtcgccc 33439 aggetggage geaatggege gatettgget eaceaeaace teeggeteee aggtteaage 33499 gattettetg ceteageete etgagtaget gggattacag etgaatgeea eettgetggg 33559 ctaatttttg tatttttagt agagatgggg tttcaccatg ttggccaggc tggcctcgaa 33619 ctectgacet egagtgatet geeegeetee tgaagtgetg ggattacagg egtgageeae 33679 ctcgtcctgg tgagggtttt ttttttccc caaccctctg tggtggatac tgaaagacca 33739 tattaggata actgtacagt atagagaagg cagtggcaag ttttctctgt catataccag 33799 agtgggcttg ggcatggtgg catactcctg tagtctcagc taatcaggag gctgaggaag 33859 gaggateget tgggeceagg agttggagae tgtagtgage tgtgateaea ceaceaeaet 33919 tcaatctggg caacagagca agagacccta tctctaaaaa aaagtaagta tttcggacac 33979 tgtgggccat acggtctctg gtgcagtttc tcaacatggc tgttgggtga acacaaccac 34039 gcacagaacg caaaccaata cacgtggctg tgggcccaga aaatgttatt tatggacaca 34099 aaaattggaa tttcatataa ctgttttgtg tcatgaaaat gatttccctt tttattttta 34159 tttttcttct caagtattta aatatgtaaa agccattttt aggcctggca ggatggttca 34219 cagctgtaat cccagcactt tgggaggtcg aggcgggagg atcacgaggt caggagatcg 34279 agaccatect ggecaacaca gtgaaacece gtetetaeta aaaatacaaa aaattaacca 34339 ggettggtgg egegetetg tagteceage tgeteaggag getgaggeag gagaateget 34399 tgaatgcagg aggcggaggt tgtagtgagc cgaggttgca ccactgcact ccagcctgag 34459 cgacagagtg agagtccgcc tcaaacaaaa aaatgtttgc ccatgctggt cttgaactcc 34519 tgggeteaag etatetgeet geettggtet eecaaagtte tgggattaca ggeatgaget 34579 acagcgcccg gacttttgtt gttttatatc tatatatcta tatataactt gttttatgta 34639 tatatataac ttgttttata tatatacata aactgcagta aaaaacatgt aacataaaat 34699 ttacettete aaacettatt aagtgeacag ttetgtgeea ttageaaatt eacactgttg 34759 gagteteaet egtegeaegg getggagtge agtggtgega teteggttea etgeaacete 34879 cacctaccag gttcaagcaa tteteetgee teageeeect eagtagetgg gattacaggt 34939 gecegtecta ecaegeceag etaatttttg tatttteagt agagaetgae tgggttteae 34999 catgttggcc aggctggtct cgaactcctg acctcaagtg atcetcccac ctcagcctcc 35059 caaagtgctg ggaatacagg catgagccac tgcgcccggc cccagaactc ttttatcttc 35119 ccaaactgaa getetgteee catgaaacae teaeteteea teeeeteeee aacteetgge 35179 acceaceatt ctactttctg teectatgaa tgtgatgget etagggaeet eetetgagtg 35239

gaatcagaca gcattttcct tttttgactg gcttatttca ctgagccaag tgcggtggca 35299 cacgcetgta ateccaaaac tttgggagac egaggeggge geateaceag aggacaggag 35359 nncgagacca geceggecaa cagggggaaa ecceateaet agggageetg cagaaagaaa 35419 gecaccacat ggectgetgg agecacacaa teccagcaaa acagggaege taaacgtagg 35479 agaaacacac aaccccagga ggcggaggtc gcagtgagcc gagatcgtgc cattacactc 35539 cagcetggge aacaagagtg aaacteegte teteetaaaa atacaaaaaa attagetggg 35599 catggtggca catgcctgta gtcccagcta cttgggaggc tgaggcagga gaatcacttg 35659 aacccgggag gtggaggttg taatgagcca aggttggcgg cgaagggatg ggtaggggcc 35719 cgagagtgac cagtetgeat eccetggeee tgegeag gg ace aac gaa tge ttg

ly Thr Asn Glu Cys Leu

295

35821 gac aac aac ggc ggc tgt tee eac gte tge aat gac ett aag ate gge Asp Asn Asn Gly Gly Cys Ser His Val Cys Asn Asp Leu Lys Ile Gly

ly 305

300

310

tac gag tgc ctg tgc ccc gac ggc ttc cag ctg gtg gcc cag cga aga 35869 Tyr Glu Cys Leu Cys Pro Asp Gly Phe Gln Leu Val Ala Gln Arg Arg 330 325 320 315

tgc gaa g gtgattteeg ggtgggaetg ageeetggge eeeetetgeg etteetgaea 35926 Cys Glu a

tggcaaccaa accectcatg cetcagttte cecatetgtt aagtgtgett gaaagcagtt 35986 aggagggttt catgagattc cacctgcatg gaaaactatc attggctggc cagagtttct 36046 tgcctctggg gattagtaat taagaaattt caggccgggt gcgtaatccc tgtaatccca 36106 acacettggg acgccgaggc gggcagatca cetgaggtcg ggagttccag accagectga 36166 ccaacatgga gaaaccccgt ctctactaaa aatacaaaat tagccgggct tggtggtgca 36226 tgcctataat cccagctact caggaggctg aggcaggaga atcacttgaa cctgggaggt 36286 ggaggttgtg gtgagccaag atcgtgccat tgcactccag cctgggcaac aagagtgaaa 36346 ctccatccaa aaaaaaaaga aaagaaaaga aaaaaaagaa aagaaatttc agctgacaca 36406 getteacact ettggttggg tteeegtggt gaatgatgag gteaggtgat gaetggggat 36466 gacacetgge tgttteettg attacatete eegagagget gggetgtete etggetgeet 36526 tcgaaggtgt gggttttggc ctgggcccca tcgctccgtc tctagccatt ggggaagagc 36586 ctecceacea ageetettte tetetettee ag at ate gat gag tgt eag gat sp Ile Asp Glu Gys Gln Asp

335

36686 ccc gac acc tgc agc cag ctc tgc gtg aac ctg gag ggt ggc tac aag Pro Asp Thr Cys Ser Gln Leu Cys Val Asn Leu Glu Gly Gly Tyr Lys 350 355 345 340

36734 tgc cag tgt gag gaa ggc ttc cag ctg gac ccc cac acg aag gcc tgc Cys Gln Cys Glu Glu Gly Phe Gln Leu Asp Pro His Thr Lys Ala Cys 370 365

36784 aag get gtg g gtgageaegg gaaggeggeg ggtgggggeg geeteaeeee Lys Ala Val g

ttgcaggcag cagtggtggg ggagtttcat cctctgaact ttgcacagac tcatatcccc 36844 tgaccgggag getgtttget eetgaggget etggeagggg agtetgeege eetgttagga 36904

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ly Ser Ile Ala Tyr Leu 375 380

tte tte ace aac egg cae gag gte agg aag atg acg etg gae egg age 38447 Phe Phe Thr Asn Arg His Glu Val Arg Lys Met Thr Leu Asp Arg Ser 385 390 395

gag tac acc agc ctc atc ccc aac ctg agg aac gtg gtc gct ctg gac 38495 Glu Tyr Thr Ser Leu Ile Pro Asn Leu Arg Asn Val Val Ala Leu Asp 400 405 410

acg gag gtg gcc agc aat aga atc tac tgg tct gac ctg tcc cag aga 38543 Thr Glu Val Ala Ser Asn Arg Ile Tyr Trp Ser Asp Leu Ser Gln Arg

415 420 425 atg atc tgc ag gtgagegteg eccetgeetg eageettgge eegeaggtga 38594

Met Ile Cys se 430

gatgagggct cetggegetg atgecettet eteeteetge eteag e ace eag ett
r Thr Gln Leu
38649

435

gac aga gcc cac ggc gtc tct tcc tat gac acc gtc atc agc aga gac 38697 Asp Arg Ala His Gly Val Ser Ser Tyr Asp Thr Val Ile Ser Arg Asp 440 445 450

atc cag gcc ccc gac ggg ctg gct gtg gac tgg atc cac agc aac atc

38745

Ile Gln Ala Pro Asp Gly Leu Ala Val Asp Trp Ile His Ser Asn Ile

455 460 465

tac tgg acc gac tct gtc ctg ggc act gtc tct gtt gcg gat acc aag 38793 Tyr Trp Thr Asp Ser Val Leu Gly Thr Val Ser Val Ala Asp Thr Lys 470 475 480

ggc gtg aag agg aaa acg tta ttc agg gag aac ggc tcc aag cca agg 38841 Gly Val Lys Arg Lys Thr Leu Phe Arg Glu Asn Gly Ser Lys Pro Arg 485 490 495

gcc atc gtg gtg gat cct gtt cat gg gtgcgtatcc acgacgctga 38887 Ala Ile Val Val Asp Pro Val His gl

500 505

gggctgcaga gggaatggag ggagcaggaa ggagcttcag gaactggtta gtgggctggg 38947 catggtggct caaagcacct gtaatcccag cactttggga ggccaaggtg ggtggatcat 39007 caagaccage etgaccaaca tggtgaaacc tegtetetae taaaaataca aaaattagee 39067 gggtgtggtg gtgggcacct gtaatcccag ctgctcggga ggctgaggca ggagaatcac 39127 ttgaacctgg gagatggagg ttgcagtgag ccaagacagc cccactgcac tccagcctgg 39187 tggctagaca acaggatggt atcttccaag cccatggctg actcagcagc tcctgggtca 39307 agacactgtg acctgtgtcc cctggcagga agcatcgccc ctgccacctg cccggtgtac 39367 tetgtacetg teaggtgaca tetgetacet aageaegtga gaggtggeat tteacagttt 39427 cagtgtggtg ctgacaaccc gggacgcaca ctgtccttgc agctacaatc aggaggtgaa 39487 tgttgggttt ccagcagaga acactggaga aggcacactt ggtgtctgga agggaaaagc 39547 agggaagaga gcatcatcag atgcctgcgg gtgaaggtgg gcccgctatg gccagcgtcc 39607 ctttttattt ttatttattt atttatttga gatggaatct cgctctgtcg cccagactgt 39667 agtgeagtgg tgegateaeg geteaetgea ageteegeet caeaggttea egeeattete 39727 ctgcctcagc ctcccgagta gctgggacta caggcacccg ccaccacgcc cggttaattt 39787 tttgcatttt tattagagac ggggtttcac cgcgttagcc aggatggtct aaatctcctg 39847 accetgtgat ceaceegect eggecteect aagtgettgg attacaageg tgagecacca 39907 egeceggeee cetttttatt ttttattttt tgagaeggag tetegetetg tegeceagge 39967 tagattgeag tggegtgate teggeteaet geageeteeg ceteceaggt teaagtgatt 40027 ctcctgcctc aacctcccaa ctaattagga ttacaagcat gtaccaccat gcctgactaa 40087 ttttttgtat ttttagtaga gactgggttt caccatgttg gctaggctgg tctcgaaccc 40147 ttagecteaa gtaatetgee tgeeteagee teecaaacag eggggattae aggeatgage 40207 cactgtgccc aacccaaccc tggatctctt ttaaacaaga caatgctcgc tgttgccaca 40267 gaacaatggg tggggtacat gtggcccagt gtgtttggcc acataactgc caggccagag 40327 ggaaagagac teteagactg tetecaetea gatacaaatg tgtgtgttgt gtgcgtgtgt 40387 tetggtetea tatttgtttg ttttgagaca gggtgteget etgteaetga gtetggagtg 40447 cagtggcgca atcagagttc actgcagcct caaactcttg ggctcagttg attctcccac 40507 tteagectee caagtagetg gaactacagg tgaacaccae tgtgeecage taatttattt 40567 tatttttagt agagatgagg teteaetatg ttgeecagge tggtettgae eteetageet 40627 caagcaatcc teetgeettg gteteceaaa gtgetgggat tacaegtgeg agceattgeg 40687 catggettgt gttettgtgt ttetteettt ttetttegag atggegtete agtetgecae 40747 ccaggetgga gtgcagtggt gtgatcatag ctcactgtag cctcaacttc ctgggetcaa 40807 geaateetet tgattteage eteeegggee tggeeageat ggtgaaaeee egtetetaet 40867

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y Phe Met Tyr Trp Thr Asp Trp 515 510

gga act ccc gcc aag atc aag aaa ggg ggc ctg aat ggt gtg gac atc 41268 Gly Thr Pro Ala Lys Ile Lys Lys Gly Gly Leu Asn Gly Val Asp Ile 530 525 520

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540 535 41367 g gtatgttege aggacageeg teccageeag ggeegggeae aggetggagg

acagacgggg gttgccaggt ggctctggga caagcccaag ctgctcctg aaggtttccc 41427 tetttetttt etttgttttt tetttttttg agatgaggte ttggtetgte acceaggetg 41487 gagtgeactg gegeaategt ageteactge ageeteeace teccaggete aagtgateet 41547 cetgeeteae ceteetgagt agetgagatt acagacaegt geeaecaegg cagactaatt 41607 ttattttatt tttgggaaga gacaaagtet tgttatgttg geetggetgg teteaaacte 41667 agggtgcaag cgatcctccc gcctcagcct tccaaactgc tgggattaca ggcgtgggcc 41727 accetaccea geeteettga agtttttetg acctgeaact eccetacetg eccattggag 41787 agggcgtcac aggggagggg ttcaggctca catgtggttg gagctgcctc tccaggtgct 41847 tttetgetag gteeetggea gggggtette etgeeeggag eagegtggee aggeeeteag 41907 gaccetetgg gactggcate ageaegtgae eteteettat ceaettgtgt gtetag 42010 at etc etc agt gge ege etc tac tgg gtt gac tec aaa ett eac tec sp Leu Leu Ser Gly Arg Leu Tyr Trp Val Asp Ser Lys Leu His Ser 560

555 550 42058 ate tea age ate gat gte aac ggg gge aac egg aag ace ate ttg gag Ile Ser Ser Ile Asp Val Asn Gly Gly Asn Arg Lys Thr Ile Leu Glu 575 570

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600 595

atc atc aac gaa gcc att ttc agt gcc aac cgc ctc aca ggt tcc gat

015859-4.ST25.2008-12-10.SEQ LISTING Ile Ile Asn Glu Ala Ile Phe Ser Ala Asn Arg Leu Thr Gly Ser Asp 615 605 610 gtc aac ttg ttg gct gaa aac cta ctg tcc cca gag gat atg gtt ctc 45313 Val Asn Leu Leu Ala Glu Asn Leu Leu Ser Pro Glu Asp Met Val Leu 625 620 ttc cac aac ctc acc cag cca aga g gtaagggtgg gtcagcccca 45358 Phe His Asn Leu Thr Gln Pro Arg g 635 640 ccccccaac ettgaaacet cettgtggaa actetggaat gttetggaaa tttetggaat 45418 45474 cttctggtat agctgatgat ctcgttcctg ccctgactcc gcttcttctg ccccag 45521 ga gtg aac tgg tgt gag agg acc acc ctg agc aat ggc ggc tgc cag ly Val Asn Trp Cys Glu Arg Thr Thr Leu Ser Asn Gly Gly Cys Gln 655 650 645 45569 tat etg tge etc eet gee eeg eag ate aac eec eac teg eec aag ttt Tyr Leu Cys Leu Pro Ala Pro Gln Ile Asn Pro His Ser Pro Lys Phe 665 670 660 45617 ace tgc gcc tgc ccg gac ggc atg ctg ctg gcc agg gac atg agg agc Thr Cys Ala Cys Pro Asp Gly Met Leu Leu Ala Arg Asp Met Arg Ser 685 680 675 tgc ctc aca g gtgtggcaca cgccttgttt ctgcgtcctg tgtcctccaa 45667 Cys Leu Thr g 690 ctgcccctc ctgagcctct ctctgctcat ctgtcaaatg ggtacctcaa ggtcgttgta 45727 aggactcatg agtcgggata accatacttt tcttggatgg acacatcagc accgggcttg 45787 acatttaccc agttcccctt tgatgcctgg tttcctcttt cccggccccc tgaagaggtg 45847 tetttatttt tttettttga gatttgetgt cacceageet ggaatgeagt ggtgecatet 45967 tggctcactg ctacctctcc cactgggttc aagcaattct cctgcctcag cctcccaagt 46027 agetgggatt acaagcatge gecaccatge etggetaagt tttgtatttt tagtacagae 46087 agggtttete catggtggce aggetggtet tgaacteetg aceteaggtg atceteceae 46147 ctetgeetee egaagtgeta egattaeagg eatgageeae egegeeeate eccetttgtt 46207 gacttttete ateetetgag aaagteteag ttgaggeeag eaceteete aagtgaattg 46267

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lu Ala Glu Ala Ala Val Ala Thr 695 700

cag gag aca tee ace gte agg eta aag gte age tee aca gee gta agg 48349 Gln Glu Thr Ser Thr Val Arg Leu Lys Val Ser Ser Thr Ala Val Arg 705 710 715

aca cag cac aca acc acc cga cct gtt ccc gac acc tcc cgg ctg cct 48397
Thr Gln His Thr Thr Thr Arg Pro Val Pro Asp Thr Ser Arg Leu Pro
720 725 730

720 725 730
ggg gcc acc cct ggg ctc acc acg gtg gag ata gtg aca atg tct cac 48445

Gly Ala Thr Pro Gly Leu Thr Thr Val Glu Ile Val Thr Met Ser His

735

740

745

caa g gtaaagactg ggccctccct aggcccctct tcacccagag acgggtccct 48499 Gln a

750

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750

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775 cagegteece caggteacag ectecegeta tgtgaceteg tgeetggetg gttgggeetg 53270 ttcacttttt eteetggaca gggaacagee eeaetggtgt cetttateae eeceaeggee 53330 teteetgget tggggetgae agtgacaaga teagacaget aaggggteag atggaggatg 53390 tggagetggg teeegtgetg tggaatagee teaeegagat ttgagtgeet tetggggaae 53450 tggttccctt gcagggggct gtgtggagag gcgcgctctc cctgcctcac ccatgctcat 53510 cetaactegg ttaccateae atetetttt tettttttte ttaaatttta agaaaaaaga 53570 aatttaattt ttttgagaga cagagtettg etetgteace caggetggag tgeagtggca 53630 ccatcatgcc tegetgcage etcaatgtet gggetcaage gateeteeca cetcageete 53690 ctgagtaget ggtgcaagec actatacece acttectatt tettaaaaag teacagecet 53750 gtgtgtgget aateetggae agaaatetag aagaagteag etaettetgg ggegtggete 53810 acccagtggg cttcaggtta gatatttctt atacttatga ggctgggtgt ggtggcttat 53870 gcctgtaatc ccagcacttt gggaggctga agtgggtgga ttgcttgggc tcaggagttc 53930 gagaccaacc tgggcaacat ggcgaaaccc tgtttctaga aaaggtacaa aaattagctg 53990 ggcaggtggc acgtgcctgt ggtaccagct acttgagggc ctgaggcagg aggatcgctt 54050 gaacctggga ggtcgaggtt gcagtgaact gagatcatgt cactgcactc cagcctggtg 54110

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780

gtc ttc ctt cta tgg aag aac tgg cgg ctt aag aac atc aac agc atc 54690 Val Phe Leu Leu Trp Lys Asn Trp Arg Leu Lys Asn Ile Asn Ser Ile 785 790 795 800

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